Guiding the developmental program of human embryonic stem cells by isolated Wnt factors

Grant Award Details

Guiding the developmental program of human embryonic stem cells by isolated Wnt factors

Grant Type: Comprehensive Grant

Grant Number: RC1-00133

Project Objective: To study how Wnt proteins influence the fate of differentiating human embryonic stem cells, and to identify conditions that promote their differentiation to definitive endoderm.

Investigator:

Name:	Roel Nusse
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $1,710,462

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: Guiding the developmental program of human embryonic stem cells by isolated Wnt factors

Public Abstract:

Just like cells in a human embryo, embryonic stem cells have the potential to give rise to all cell types and tissues in a human body. That is why it is an exciting prospect to use these cells in tissue repair. But in order to do so, we have to understand how we can guide the differentiation of stem cells. For example, if one wants to use stem cells for replacing defective insulin-producing cells in the pancreas, we have to learn how we can convert stem cells into pancreas cells, or at least precursors to pancreas cells. So the question is then, how do cells in an embryo become different from each other? Research done in animals has shown that there are signaling proteins that instruct cells to change from one type into another. One important group of these signaling proteins are the Wnts. Studied in our lab for along time, Wnts are powerful differentiation factors. To use Wnt proteins as factors under controlled conditions, one has to be able to isolate them. This has been a major problem in the past, but we have solved this recently. We are therefore now in a position to test how Wnt proteins, when added to stem cells, change the state of differentiation of the cells and our preliminary results indicate that there are indeed significant consequences. A second question we want to address is how we can recognize intermediate stages in stem cell differentiation. Going from a stem cell to a pancreatic insulin-producing cell is a step-wise process, following a road map where we know the beginning and the end but not the steps in between. We intend to perform gene-chip experiments to chart those steps and to map the pathways that stem cells follow to differentiated progeny cells. Finally, we will focus our research on promoting the differentiation of stem cells into endoderm, a tissue that is the precursor to pancreas development. We expect this research to contribute significantly to our insights into stem cell behavior, but also to generate new tools to improve the use of stem cells for regenerative medicine.

Statement of Benefit to California:

This research will lead to new tools to control the differentiation pathways of human embryonic stem cells. More specifically, the work aims at generating an important class of differentiation factors, the Wnts, that are known to influence how cells in an embryo differentiate. Despite the potential of Wnts in stem cell research, their practical use has been limited because the proteins were difficult to purify. Our lab has solved this problem and we will therefore explore their use. Our experiments will include adding the factors to stem cells and to test how they differentiate, in particular into endoderm, cells that are the direct precursors of the pancreas, liver, lungs and other medically-important organs. As we have done in the past, the products of the work, including the Wnt factors, will be made available to other researchers. This work will generate fundamental biological insights into how stem cells differentiate. In turn, this new knowledge should accelerate efforts to use HESC for regenerative medicine.
